

LISTING OF THE CLAIMS

The claims as pending are as follows:

1. (Previously presented) A method of analyzing the methylation state of one or more nucleotide sequences comprising the steps of:

a) selecting one or more genomic test nucleotide sequences from one or more subjects that exhibit a phenotype of interest, and one or more corresponding genomic control sequences from one or more control subjects that lack the phenotype of interest;

b) digesting the genomic test nucleotide sequences and separately digesting genomic control sequences with one or more methylation-sensitive restriction endonucleases that cut unmethylated sequences but not methylated sequences, to produce ends that can be ligated to an adaptor nucleotide sequence;

c) ligating adaptor nucleotide sequences to the ends produced from step b) to produce ligated sequences;

d) cleaving the ligated sequences with one or more methylation-specific endonucleases that cut methylated sequences but not unmethylated sequences, to produce amplifiable test nucleotide sequences, non-amplifiable nucleotide sequences, amplifiable control nucleotide sequences and non-amplifiable control nucleotide sequences;

e) amplifying the amplifiable test nucleotide sequences and amplifiable control nucleotide sequences to produce amplified test nucleotide sequences and amplified control nucleotide sequences;

f) labeling the amplified test nucleotide sequences from step e) with a first label, and labeling the amplified control nucleotide sequence from step e) with a second label;

g) hybridizing the labeled products of step f) with an array comprising a series of nucleotide sequences that are capable of hybridizing thereto; and

h) determining the ratio of the signals emitted by the first label relative to the second label for each hybridized nucleotide sequence on the array.

2. (Previously presented) The method of claim 1, further comprising a step of correcting for the

effect of DNA sequence variation:

i) amplifying the genomic test nucleotide sequences and separately amplifying the genomic control sequences with a DNA polymerase to produce an unmethylated copy of the genomic test nucleotide sequences and an unmethylated copy of the genomic control sequences;

ii) treating the unmethylated copy of the genomic test nucleotide sequences and separately treating the unmethylated copy of the genomic control sequences with restriction endonuclease digestion, adaptor ligation, amplification, labeling, array hybridization, and ratio determination steps that are equivalent to corresponding steps b), c) and e-h); and

iii) comparing the one or more ratios determined in step ii) to the one or more ratios determined in step h).

3. (Canceled)

4. (Previously presented) The method of claim 1, wherein the methylation specific endonuclease is McrBC.

5. (Previously presented) The method of claim 1, wherein the methylation-sensitive restriction endonuclease comprises HpaII, BsuI51 (ClaI), Hin6I, AclI (SsiI), TspI, or any combination thereof.

6. (Previously presented) The method of claim 1, wherein step f) further comprises labeling the non-amplified test nucleotide sequences from step d) with the first label, and labeling the non-amplified control nucleotide sequences from step d) with a second label.

7. (Previously presented) The method of claim 1, wherein the phenotype of interest comprises cancer, diabetes, Alzheimer's disease, or schizophrenia, multiple sclerosis, psoriasis, atherosclerosis, asthma, autism, or rheumatoid arthritis.

8. (Previously presented) The method of claim 1, wherein the first label, second label or both are

chemically reactive fluorophores.

9. (Previously presented) The method of claim 1, wherein said chemically reactive fluorophores are independently Cy 3 or Cy 5.

10-19. (Canceled)

20. (Withdrawn, Previously presented) A kit comprising one or more genomic test nucleotide sequences, one or more corresponding genomic control nucleotide sequences, one or more frequent cutting restriction endonucleases, one or more specific adaptor nucleotide sequences, one or more methylation-sensitive restriction endonucleases, one or more CpG specific restriction endonucleases, one or more probes for labeling the nucleotide sequences, one or more microarrays capable hybridizing to the genomic test and control nucleotide sequences, software for displaying and/or analyzing the sequences labeling to the microarray, reagents and/or enzymes for amplifying nucleotide sequences, or any combination thereof.

21. (Previously presented) A method of identifying DNA sequence variation in a methylation-state-analysis of one or more nucleotide sequences comprising the steps of:

a) selecting one or more genomic test nucleotide sequence from one or more subjects that exhibit a disease phenotype of interest and one or more corresponding genomic control sequences from one or more control subjects that lack the disease phenotype of interest;

b) amplifying the genomic test nucleotide sequences and separately amplifying the genomic control sequences with a DNA polymerase, to produce an unmethylated copy of the genomic test nucleotide sequences and an unmethylated copy of the genomic control sequences;

c) treating the unmethylated copy of the genomic test nucleotide sequences and separately treating the unmethylated copy of the genomic control sequences with restriction endonuclease digestion, adaptor ligation, amplification, labeling, array hybridization, and ratio determination steps , and;

d) comparing the one or more ratios determined in step c) to the one or more ratios of the

methylation-state-analysis, thereby identifying DNA sequence variation in the methylation-state-analysis.

22. (Canceled)